REMARKS

Reconsideration and withdrawal of all rejections of the application, and allowance of the claims, especially in view of the remarks herein, are respectfully requested, as this paper places the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Attached hereto is a substitute specification as Exhibits A and B. Exhibit A is the substitute specification with markings to show all the changes relative to the immediate prior version. Exhibit B is a clean version of the substitute specification. The herein amendments to the specification address the objections to the specification and the abstract. The substitute specification includes no new matter.

Claims 4-12 and 14-31 were pending in the present application. Claims 4-12 and 14-27 are cancelled without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. Claims 28-31 are under consideration in this application. Claim 28 has been amended to recite "and/or" instead of "or and". Furthermore, item (b) has been deleted from the claim and the language changed accordingly thereby eliminating any need to bring the claim into compliance with Markush language. Claim 29 has been amended to recite to "amino acid" instead of "amino-acid". Claim 31 has been amended to recite to "an" expression system. Moreover, claim 31 now recites to "An isolated" host cell, rather than "A cell".

No new matter is added by these amendments.

This response is made in an earnest effort to advance prosecution of this application and to place the claims in a condition for allowance or in a better condition for appeal, and are made without prejudice, admission, surrender of subject matter, or any intention of creating estoppel as to equivalents. The right to file divisional applications directed to the broader claims as they existed prior to the entry of this response is expressly reserved.

The Examiner is thanked for withdrawing previous objections to the claims and the previous rejections under 35 U.S.C. § 112, first paragraph, to the claims.

It is submitted that these claims are patentably distinct from the prior art cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments and remarks herein are not made for the purpose of patentability within the

meaning of 35 U.S.C. §§101, 102, 103 or 112; but rather the amendments and remarks are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support for the amended recitations in the claims is found throughout the specification.

II. OBJECTIONS TO THE SPECIFICATION

The Examiner objected to the specification because pages 42-46 "seemed to list claims" that were referred to throughout the specification by "paragraphs". Applicants specifically addressed this in its last response. Applicants maintain that the paragraphs in this section are not claims, are not intended to be claims, but rather are numbered paragraphs which form part of the description of the invention. Applicants reiterate its position in its last response, that it is not aware of any rule prohibiting the use of such numbered paragraphs in the description of the invention. Therefore, although applicants disagree with the objection, in the interest of expediting prosecution the following amendments have been made to the specification: On page 42, the following text has been deleted: "The invention will now be further described by the following numbered paragraphs". In addition, all of the remaining text following this sentence in the section entitled "Best Mode for Carrying Out the Invention", up to page 46, has also been deleted. The additional references made to "paragraphs" throughout the specification, pages 5-9, remain in the specification for the reasons above. If this is the only issue which prevents a Notice of Allowance from being issued, the applicants authorize the insertion of the text represented by the paragraphs via Examiner's Amendment.

No new matter is added by the amendments to the specification.

A. Objections to the drawings

Attached hereto as Exhibit C is a copy of the Petition under 37 C.F.R. 1.84(2), which was submitted in partial response to the Office Action of May 3, 2005 to be filed concurrently with the Amendment and Request for Extension of Time to the same. In addition, also attached as part of Exhibit C is a copy of the check submitted for payment for petition of acceptance of colored drawings as well as a copy of the receipt postcard from the Patent and Trademark Office, dated September 2, 2005.

Accordingly, in view of the above remarks, reconsideration and withdrawal of the objections to the drawings is respectfully requested.

B. Objections to the abstract

The abstract was objected to because of language problems. In response, the abstract has been amended to correct such informalities.

In view of the above amendments, reconsideration and withdrawal of the objections to the abstract is respectfully requested.

III. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

A. Written Description

Claims 28-29 and 31 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is traversed.

The Office Action alleges that the claims are directed to an isolated DNA molecule contained in (SEQ ID NOS:1, 3, or 5), a complementary sequence or a variant sequence comprising all or a part of the DNA molecule or complement thereof, and to a variant hybridizing to the claimed DNA, complement or a probe, wherein said variant encodes a protein that binds to Filamin 1 and inhibits cell migration. The Examiner objects that claims 28-29 and 31 do not set forth the specific hybridization conditions considered to be stringent, thereby including sequences that may hybridize to the sequence of interest but may not necessarily encode the same protein.

The amended version of claim 28 is adequately described under Example 9 of the Synopsis of Application of Written Description Guidelines. 66 Fed. Reg. 1099, January 5, 2001. Both structure (*i.e.* the sequence) and function (*i.e.* root specific promoter activity) of the claimed molecule are provided, and stringent hybridization conditions are defined in the paragraph bridging pages 11 and 12 of the substitute specification.

Therefore, claim 28 is drawn to a genus of nucleic acids, all of which must hybridize with SEQ ID NOS:1, 3, or 5 under specified conditions and must have a specific recited activity. A person of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the stringent hybridization conditions required by claim 28 yield structurally similar nucleic acid molecules. Thus a representative number of species is disclosed, since the structure and function requirements are both satisfied,

and the level of skill and knowledge in the art are adequate to determine that the inventors were in possession of the claimed invention.

Claims 28-31 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office Action alleges that the claimed invention is directed to an isolated DNA molecule, a complement thereof and variant thereof, and that the claims encompass a large genus that has not been adequately described. The rejection was based upon the recitation in the claims of "comprising". This recitation has been removed. The amended version of claim 28 now recites to a variant "consisting essentially of" the claimed sequences that hybridizes with a probe consisting of nucleotide positions 1289-1453 of SEQ ID NO: 1 under stringent conditions, and wherein the variant sequence encodes a protein that binds to Filamin 1 and inhibits cell migration.

Moreover, the specification provides actual reduction to practice for a "representative number of species" of FILIP variants having various regions various regions added or deleted while retaining Filamin-1 binding activity including L-FILIP (amino acid residues 1-1212), S-FILIP (comprising only amino acid residues 248-1212 of L-FILIP), FILIPΔN (a FILIP variant having the N-terminal leucine zipper region deleted and containing only amino acid residues 755 to 1212 of L-FILIP, see page x), h-FILIP (a human ortholog of L-FILIP), L-FILIP-GFP (L-FILIP with added amino acids encoding the GFP-protein), S-FILIP-GFP (S-FILIP with added amino acids encoding the GFP-protein), FILIPΔN -GFP (FILIPΔN with added amino acids encoding the GFP-protein).

The specification also provides a demonstration of a FILIP variant that does not have the claimed Filamin 1 binding activity, namely S-FILIPΔC-GFP (C-terminus deficient FILIP), Figure 2b.

The MPEP states that *"[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed,"* and also states that *"[d]escription of a representative number of species does not require the description to be of such specificity that it*

would provide individual support for each species that the genus embraces". (MPEP §2163).

Given the high level of skill in the field of art of the present invention (i.e. the field of molecular neuroscience), the specification does disclose a "representative number of species" of the genus of FILIP variants, and does disclose a number of species sufficient that one of skill in the art would recognize that the Applicants were in possession of the novel Filamin-1 binding proteins recited in the claims.

In addition, the nucleic acids recited in the new claims exhibit the physical property of hybridizing under stringent conditions with the S-FILIP (SEQ ID NO: 1), L-FILIP (SEQ ID NO:3), or h-FILIP (SEQ ID NO: 5) sequences, or with a probe consisting of nucleotide positions 1289-1453 of SEQ ID NO: 1. Furthermore, the nucleic acids recited in the new claims encode proteins that have the functional property of binding to Filamin 1. The specification discloses a correlation between the function of the claimed FILIP proteins and their Filamin 1 binding function. The specification demonstrates that the C-terminal region of the FILIP proteins is required for binding to Filamin-1 since a FILIP variant having the N-terminal region deleted (FILIPΔN) retains the ability to bind to Filamin 1, whereas a FILIP variant having the C-terminal region deleted (S-FILIPΔC-GFP) does not bind to Filamin 1.

Therefore, the amended claims presented herein satisfy the written description requirements of 35 U.S.C. §112, first paragraph.

B. Enablement

Claims 28-31 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the DNA encoding proteins set forth in SEQ ID NOS:2, 4 and 6 that controls cell migration and cell death, does not reasonably provide enablement for any variant thereof of the claimed DNA. Specifically, the Office Action asserts that undue experimentation would be required to practice the invention since the claims encompass a large amount of variability for the DNA and the encoding protein sequence and there is no correlation made between the structure and function of the claimed products following modification. Moreover, the Office Action asserts that the large variability of DNA contemplated may encode a protein that will not bind Filamin 1. The rejection is based on the lack of description of properties of the claimed variants and lack of demonstration that any such variant retains the activity. Furthermore, the Examiner objects to the recitation in claim 28 "part or all of either of

these sequences" and the functional limitation of "encodes a protein that binds Filamin 1 and inhibits cell migration". The rejection is traversed.

The amendments presented herein to claims 28-31 satisfy the enablement requirements of 35 U.S.C. §112, first paragraph. The new claims do not encompass a large amount of variability for the claimed DNA and the encoding protein sequences. Instead, the new claims encompass only those DNA molecules that consist essentially of variant sequences that hybridize under stringent conditions to SEQ ID NOS: 1, 3, and/or 5, or hybridize under stringent conditions with a probe consisting of nucleotide positions 1289-1453 of SEQ ID NO: 1; in addition, the variant sequence encodes a protein that binds to Filamin 1 and inhibits cell migration.

The Office Action also asserts that undue experimentation would be required to practice the present invention. Applicants respectfully disagree. It would not require undue experimentation for one of skill in the art to practice the invention using FILIP variants having the physical and functional properties recited in the new claims.

The MPEP states that *"[a] patent need not teach, and preferably omits, what is well known in the art"* (MPEP §2164.01, citing, *inter alia*, *In re Buchner*, 929 F.2d 660, 661, (Fed. Cir. 1991)). The MPEP also states that *"[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation"*. (MPEP §2164.01). The level of skill in the art in the field of molecular neuroscience is high, and the art typically engages in experimentation that involves making and/or screening for and/or selecting mutants or variants of proteins. Thus, it would not involve undue experimentation for one of skill in the art to make and/or screen for and/or select mutants or variants of the recited FILIP proteins or the nucleic acids that encode them.

The MPEP states that the specification is enabling where there is considerable direction and guidance in the specification; where there is "a high level of skill in the art at the time the application was filed; and where all of the methods needed to practice the invention were well known." (See MPEP §§2164.0 citing *In re Wands*, 858 F.2d at 740, 8 USPQ2d at 140).

The Examiner's attention is respectfully invited to some case law under the first paragraph of Section 112. First, it is a well known principle that claims must be read in light of the specification. See In re Marosi, 710 F2d 799, 218 USPQ 289 (Fed. Cir. 1983). Second, it has been determined that the claims need not be limited to preferred embodiments in the specification. It is improper, according to In re Goffe, 191 U.S.P.Q. 429, 431 (CCPA 1976), to

limite the claims of an application to the specific examples in the specification under the guise of lack of enablement:

> To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials . . . would not serve the constitutional purpose of promoting, progress in the useful arts.

Third, it is urged that the subject matter in the claims is not broader than the enabling disclosure. Applicants respectfully submit that the claims are more than adequately supported by the specification. There is no particular number of examples which makes specific claim language adequate or enabled. Indeed, enablement is not even related to the number of examples in the specification. In In re Borkowski, 164 USPQ 642, 646 (CCPA 1972), the court stated:

> There is no magical relation between the number of representative examples and breadth of the claims . . . the number and variety of examples are irrelevant if the disclosure is 'enabling' and sets forth the 'best mode contemplated'.

Moreover, "the laws does not require a specification to be a blueprint in order to satisfy the requirement for enablement under 35 USC §112". Staehelin v. Secher, 24 USPQ2d 1513, 1516 (Bd.Pat.App.&Int. 1992) Indeed, a specification need not disclose–and best omits—that which is well known in the art. In re Buchner, 929 F2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991)

The Examiner is also respectfully reminded that it has been held that the specification must be accepted as enabling of the invention under 35 U.S.C. §112, unless doubt as to the truth/accuracy of the statements made with the specification is raised. In re Marzocchi, 169 U.S.P.Q. 367 (CCPA 1971):

> It is incumbent upon the Patent Office . . . to explain why it doubts the truth or accuracy of any statements in supporting disclosure and to backup assertions of its own with acceptable evidence or reasoning which is inconsistent with the contended statements.

The level of skill in the art of molecular neuroscience is high, and was high at the time when the present application was filed. For example, it would have been well known to one skilled in the art at the time of the invention, how to determine if a given nucleotide sequence hybridizes with another under high stringency conditions. Moreover, the specification of the

present application provides considerable guidance as to how to test whether a given variant protein has the recited features. For example, the specification teaches how to determine whether a given protein binds to Filamin-1 using the yeast two-hybrid assay, how to determine whether a given protein binds to Filamin-1 using immuno-precipitation assays, and how to determine whether a given protein co-localizes with Filamin-1 using immunocytochemistry. (See Example 2, starting on page 34 of the specification). All of these assays are routinely practiced by those skilled in the art, and do not require undue experimentation. The specification also describes how to determine whether FILIP proteins or FILIP variant proteins, have an effect on cell migration by teaching how to determine cell migration rate in FILIP-transfected cells, and how to measure lamellipodium formation (correlated with cell migration ability) using *in vitro* wound healing assays. These assays are also routinely practiced by those skilled in the art and do not require undue experimentation.

Accordingly, in view of the above remarks, reconsideration and withdrawal of the rejections of the claims under 35 U.S.C., first paragraph, is respectfully requested.

IV. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 28-31 under 35 U.S.C. §112, second paragraph, for allegedly failing to set forth the subject matter which the applicant(s) regard as their invention. Specifically, the Examiner asserts that claim 28 is indefinite because it recites to a variant that has all of the sequences in the complement, and the complement of the encoding DNA cannot encode the same protein. Claim 28 has been amended so that it no longer recites to a variant that has all of the sequences in the complement. This amendment obviates the rejection.

Furthermore, the Examiner rejected claim 28 because it recites to "stringent hybridization conditions" without setting forth what conditions are deemed to be stringent thereby leaving the metes and bounds of the claim undefined. The rejection is traversed.

Applicants respectfully disagree that the term "hybridization under stringent conditions" in the claims would not enable one skilled in the art to make and/or use the invention. One skilled in the art would understand under what stringent conditions hybridization of the two DNA molecules would occur, based on the disclosure in the application in combination with his/her knowledge in the art. "Stringent hybridization conditions" are defined in the paragraph bridging pages 11 and 12 of the substitute specification.

Furthermore, the term "stringent conditions" is clearly defined in the literature relied upon by one skilled in the art. Stringent conditions for hybridization are mentioned in numerous laboratory handbooks, for example, Molecular Cloning: A Laboratory Manual, Maniatis et al. (1989). Further, particularly stringent hybridization conditions are not required to practice the instant invention.

Furthermore, the term "hybridization under stringent conditions" is a widely used term in the biotechnology area and has been an acceptable term in a large number of biotech patents. The U.S.P.T.O. has granted numerous patents with claims using the term "stringent conditions" to describe hybridization conditions, whether or not specific hybridization conditions are provided in the specification.

For example, the Examiner's attention is respectfully invited to U.S. patent numbers 5,587,290, 5,492,811, 5,650,276, and 5,312,909.

Claims 5 and 6 of U.S. Patent Number 5,587,290 (the '290 patent) are directed to an isolated nucleic acid comprising ATH1 or a fragment capable of hybridizing under stringent conditions to ATH1.

The specification of the '290 patent states:

> "The subject nucleic acids include ATH1 probes and primers comprising one or more ATH1 fragments capable of hybridizing with ATH1 under stringent conditions, e.g. under stringency conditions characterized by a hybridization buffer comprising 0% formamide in 0.9M saline/0.09M sodium citrate (SSC) buffer at a temperature of 37° C. and remaining bound when subject to washing at 42° C. with the SSC buffer at 37° C. Preferred nucleic acids will hybridize in a hybridization buffer comprising 20% formamide in 0.9M saline/0.09M sodium citrate (SSC) buffer at a temperature of 42° C. and remaining bound when subject to washing at 42° C. with 2xSSC buffer at 42° C." (see, col. 3, lines 45-57).

There is no further disclosure related to the stringent hybridization conditions.

Claims 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, and 43 of U.S. Patent Number 5,492,811 describe an isolated DNA molecule containing a first strand and a second strand which hybridize under stringent hybridization conditions with said first strand. The specification merely discloses that "the extent of hybridization is accomplished by means appropriate and conventionally utilized for this purpose" (see, col. 2, lines 16-21) and examples II and III state that modifications of standard or conventional hybridization procedures are employed. There is no disclosure of any particular hybridization conditions, nor is the term "stringent conditions" used

in the specification. Nonetheless, the phrase "hybridizing under stringent conditions" is used in the issued claims.

Claim 14 of U.S. Patent Number 5,650,276 is directed to a method wherein the presence of or the amount of a polypeptide is determined using a nucleic acid probe that hybridizes, under stringent conditions, with RNA transcribed from a cellular gene. The specification defines "stringent conditions" as "conditions in which non-specific hybrids will be eluted but at which specific hybrids will be maintained" (col. 3, lines 49-51). The remainder of the specification is completely silent as to hybridization conditions.

Similarly, U.S. Patent Number 5,312,909 is directed to a recombinant DNA comprising a gene coding for neutral trehalase of yeast which consists of DNA capable of hybridizing under stringent conditions to a DNA insert in plasmid TRE 6.1.1. The specification refers to Maniatis et al; Molecular Cloning, A Laboratory Manual (1982), pp. 387-389 for the definition of "stringent conditions" (see, col. 4, lines 33-36). The remainder of the specification is silent as to the stringent hybridization conditions.

Applicants respectfully submit that the U.S.P.T.O. has recognized the term "stringent hybridization conditions" as a term known in the art. The particular stringent conditions do not have to be provided in the specification in order to include the term in the claims.

V. REJECTIONS UNDER 35 U.S.C. §101

Claim 31 was rejected under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Specifically, the Office Action asserts that claim 31 is drawn to a naturally occurring product. Claim 31 has been amended to recite to "An isolated" host cell rather than "A" cell, to indicate a product not found naturally in nature. This amendment obviates the rejection. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

VI. REJECTIONS UNDER 35 U.S.C. §102(b)

Claims 28, 29, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Dyson et al. based on the broad recitation of a variant sequence amino acids are deleted, substituted or added; a sequence comprising part or all of either of the sequences in item (a-b) of claim 28. The Office Action asserts that Dyson et al. disclose a DNA encoding a protein, which binds filamin, thus reads on the claims. The rejection is based on the language "all or part of" in claim 28 because allegedly, the structure disclosed in the reference would hybridize to the claimed sequences set forth in SEQ ID NOS:1, 3 or 5. The Office Action further asserts that Dyson

teaches expression in a host cell, thereby anticipating claim 31. Therefore, the Examiner asserts, the limitations of the claims are met by this reference. The rejection is traversed.

Claims 28-31 as presented herein are not anticipated by Dyson et al. Claim 28 now recites to a variant sequence consisting essentially of either of the sequences set forth in SEQ ID NOS:1, 3, or 5 wherein the variant sequence hybridizes with the sequences recited in SEQ ID NOS:1, 3, or 5 under stringent conditions, or hybridizes with a probe consisting of nucleotide positions 1289-1453 of SEQ ID NO:1 under stringent conditions, and wherein the variant sequence encodes a protein that binds to Filamin 1 and inhibits cell migration.

Dyson discusses a phosphoinositidylinositol 3,4,5 triphosphate 5-phosphatase, SHIP-2, because SHIP-2. SHIP-2 binds filamin, however Dyson does not teach or disclose that SHIP-2 inhibits cell migration. In fact, Dyson discusses SHIP-2 as a 5-phosphatase which plays a significant role in negatively regulating insulin signaling. Dyson discusses a few other functions of SHIP-2 however nowhere does Dyson teach that SHIP-2 has a role in cell migration, as recited in the present claims. Accordingly, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §102(b) is respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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